FDA Oncology Update

This section provides a brief overview of new cancer drugs and new indications approved by the FDA between July 30 and September 26, 2019.

NEW DRUGS

Nubeqa, Oral Androgen Receptor Inhibitor, Approved for Nonmetastatic Prostate Cancer

On **July 30, 2019**, the FDA approved darolutamide (Nubeqa; Bayer HealthCare), an oral androgen receptor inhibitor, for the treatment of patients with nonmetastatic castration-resistant prostate cancer (CRPC).

"Patients at this stage of prostate cancer typically don't have symptoms of the disease. The overarching goals of treatment in this setting are to delay the spread of prostate cancer and limit the burdensome side effects of therapy," Matthew Smith, MD, PhD, Director, Genitourinary Malignancies Program, Massachusetts General Hospital Cancer Center, said in a statement.

A total of 1509 patients with nonmetastatic CRPC were randomized to darolutamide or to placebo. All patients also received a gonadotropin-releasing hormone analog unless they previously had a bilateral orchiectomy. The median metastasis-free survival was 40.4 months with darolutamide versus 18.4 months with placebo (P <.0001). The overall survival data were not yet mature at the FDA approval.

The most common (≥2%) adverse events were fatigue, extremity pain, and rash. Ischemic heart disease (4.3%) and heart failure (2.1%) were more common with darolutamide than with placebo.

Turalio First FDA-Approved Systemic Therapy for Tenosynovial Giant-Cell Tumor

On **August 2, 2019**, the FDA approved pexidartinib (Turalio; Daiichi Sankyo) capsules, a kinase inhibitor, for adults with symptomatic tenosynovial giant-cell tumor (TGCT), representing the first systemic therapy approved for patients with TGCT.

A total of 120 patients were randomized to pexidartinib or to placebo. After 25 weeks, the overall response rate with pexidartinib was 38%, including 15% complete responses and 23% partial responses, versus no responses with placebo (P <.0001). Overall, 22 patients with a response to pexidartinib therapy maintained the response for ≥6 months. In addition, 13 patients maintained the response for ≥12 months.

The most common side effects were increased lactate dehydrogenase, increased aspartate aminotransferase, hair color changes, increased alanine aminotransferase, and increased cholesterol. Pexidartinib was approved with a boxed warning about the risk for fatal liver injury; the drug is only available through a Risk Evaluation and Mitigation Strategy program.

Rozlytrek Approved for All Patients with *NTRK* Fusion Tumors and for Metastatic NSCLC with *ROS1* Mutation

On **August 15, 2019**, the FDA accelerated the approval of entrectinib (Rozlytrek; Genentech), an oral kinase inhibitor, for the treatment of adults and adolescents whose cancer involves neurotrophic tyrosine receptor kinase (*NTRK*) gene fusion that has no effective treatments. This is the third cancer drug approved by the FDA based on a common biomarker and the second drug for patients with *NTRK* gene fusion.

"We're seeing continued advances in the use of biomarkers to guide drug development," said FDA Acting Commissioner Ned Sharpless, MD.

The 4 clinical trials included 54 adults with *NTRK* fusion–positive tumors. The overall response rate (ORR) with entrectinib was 57%, including 7.4% complete responses; 61% of the overall responses lasted ≥9 months. The most common cancer sites were the lung, salivary gland, breast, thyroid, and colon/rectum.

At the same time, the FDA approved entrectinib for the treatment of adults with metastatic non–small-cell lung cancer (NSCLC) and a *ROS1* mutation, based on the 51 adults with *ROS1*-positive NSCLC in the studies. The ORR for those patients was 78%, including 5.9% complete responses; the responses lasted ≥12 months in 55% of those patients.

The most serious effects were congestive heart failure, central nervous system effects, skeletal fractures, hepatotoxicity, hyperuricemia, QT prolongation, and vision disorders.

Inrebic Receives FDA Approval for Adults with Myelofibrosis

On **August 16, 2019**, the FDA approved fedratinib (Inrebic; Celgene), an oral kinase inhibitor, for adults with

Copyright © 2019 by Engage Healthcare Communications, LLC; protected by U.S. copyright law.
Photocopying, storage, or transmission by magnetic or electronic means is strictly prohibited by law.

intermediate-2 or high-risk primary or secondary—post–polycythemia vera or post–essential thrombocythemia—myelofibrosis, a rare bone marrow disorder.

This approval was based on a phase 3, double-blind, randomized, placebo-controlled clinical trial of 289 patients who were randomized to 400 mg or 500 mg of fedratinib or to placebo, once daily, for at least 6 cycles.

Of the 96 patients who received 400 mg of fedratinib, 35 achieved a ≥35% reduction in spleen volume (the primary end point) versus 1 patient who received placebo (P <.0001). The median duration of spleen response was 18.2 months with the 400-mg dose; and 40% of patients who received that dose had a ≥50% reduction in myelofibrosis-related symptoms versus 9% with placebo.

The most common (≥20%) side effects were diarrhea, nausea, anemia, and vomiting. Fedratinib was approved with a boxed warning about the risk for serious and fatal encephalopathy, including Wernicke's encephalopathy.

NEW INDICATIONS

Erleada Approved for Metastatic Castration-Sensitive Prostate Cancer

On **September 17, 2019**, the FDA approved a new indication for apalutamide (Erleada; Janssen Biotech) for the treatment of patients with metastatic castration-sensitive prostate cancer (CSPC). Apalutamide was initially approved in 2018 for nonmetastatic castration-resistant prostate cancer.

This new indication was approved based on a randomized, double-blind, placebo-controlled clinical trial of 1052 patients with metastatic CSPC who were randomized to apalutamide or to placebo. All patients also received androgen-deprivation therapy (ADT).

At a prespecified interim analysis, the hazard ratio (HR) for overall survival (OS) was 0.67 (95% confidence interval [CI], 0.51-0.89; P = .005); a median OS was not reached in either arm. The radiographic progression-free survival (PFS) was HR 0.48 (95% CI, 0.39-0.60; P <.0001). The median radiographic PFS was not reached in the apalutamide (plus ADT) arm versus 22.1 months in the placebo (plus ADT) arm.

The most common (≥10%) side effects with apalutamide were fatigue, arthralgia, rash, decreased appetite, fall, decreased weight, hypertension, hot flushes, diarrhea, and fracture.

Keytruda-Lenvima Combo Approved for Advanced Endometrial Carcinoma

On **September 17, 2019**, the FDA accelerated the approval of a new combination of pembrolizumab (Keytruda; Merck) plus lenvatinib (Lenvima; Eisai) for advanced endometrial carcinoma that is not associated with microsatellite instability high (MSI-H) or mismatch repair–deficient (dMMR) tumors in patients whose disease progressed after systemic therapy and who are candidates for curative surgery or radiation.

The approval of this combination was based on a single-arm, multicenter, open-label, multicohort clinical trial of 108 patients with metastatic endometrial carcinoma that had progressed after ≥1 systemic therapies. Of the 108 patients, 94 had non–MSI-H or non-dMMR tumors, 11 had MSI-H or dMMR tumors, and 3 had unknown MSI-H or dMMR status.

The objective response rate in those without MSI-H or dMMR tumors was 38.3%, including 10.6% complete responses and 27.7% partial responses. The median duration of response was not reached at the time of data cutoff, and 69% of the responses lasted ≥6 months.

Side effects with this combination were similar to those seen with each treatment.

Daratumumab Combination Approved for First-Line Treatment in Transplant-Eligible Patients with Multiple Myeloma

On **September 26, 2019**, the FDA approved the combination of daratumumab (Darzalex; Janssen Biotech) with bortezomib (Velcade), thalidomide (Thalomid), and dexamethasone, for first-line treatment of multiple myeloma in patients eligible for autologous stem-cell transplant (ASCT). In June 2019, the FDA approved daratumumab plus lenalidomide (Revlimid) and dexamethasone for patients with newly diagnosed multiple myeloma who are ineligible for ASCT.

This current new indication was based on an open-label, randomized phase 3 clinical trial comparing induction and consolidation therapy with daratumumab plus bortezomib, thalidomide, and dexamethasone (DVTd) versus bortezomib, thalidomide, and dexamethasone (VTd) in ASCT-eligible patients with newly diagnosed multiple myeloma.

At a median follow-up of 18.8 months, the median progression-free survival had not been reached in either arm. However, DVTd reduced the risk for disease progression or death by 53% versus VTd (P <.0001). At day 100 post-ASCT, the stringent complete responses were 28.9% with DVTd versus 20.3% with VTd.

The most common (≥20%) adverse events were infusion reactions, peripheral sensory neuropathy, constipation, asthenia, nausea, peripheral edema, neutropenia, thrombocytopenia, pyrexia, and paresthesia. There were no significant differences in the number or type of serious adverse events in the 2 arms.

Copyright © 2019 by Engage Healthcare Communications, LLC; protected by U.S. copyright law.
Photocopying, storage, or transmission by magnetic or electronic means is strictly prohibited by law.